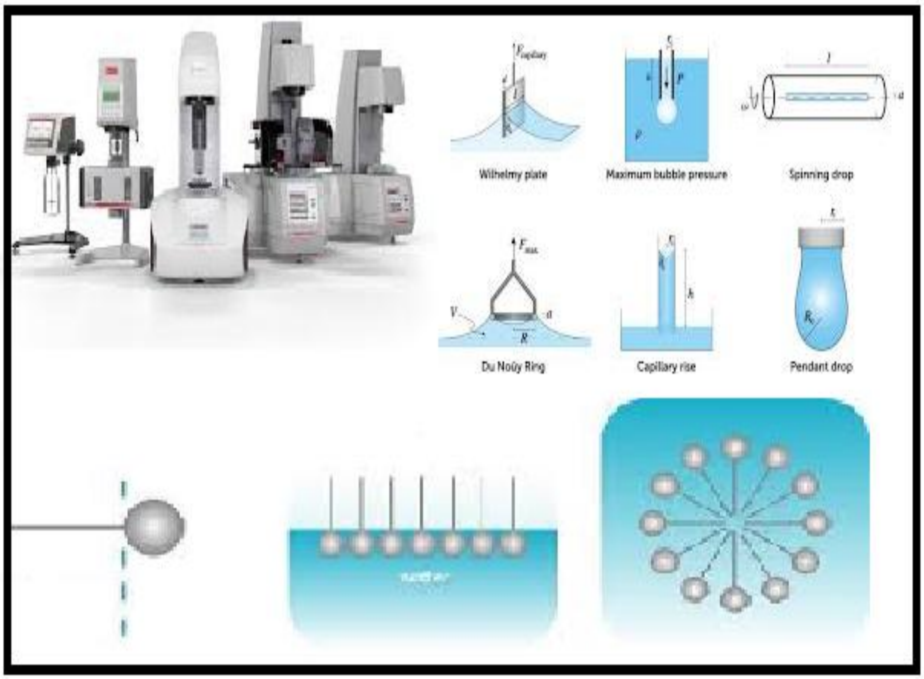
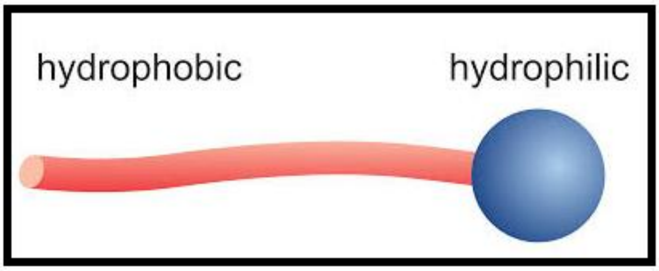
كلية الصيدلة جامعه طيبه

College of Pharmacy
Taibah University

Pharmaceutics I (PPT 241)

Practical Handout





Taibah University

College of Pharmacy

Department of Pharmaceutics and Pharmaceutical Technology

Practical Handout

Student Name: ……………………………………………………………………

Student ID number: ……………………………………………………………

Instruction to the students

This Practical handout contains 5 marks based on:

1. Clothes/Lab coat (1 mark)
2. Procedure steps (2 marks)
3. Results (1/2 mark)
4. Viva (1 Question) (1/2 mark)
5. Cleaning the working area (1 mark)

While in the Lab

- Wear a clean & tidy Lab coat.
- Handle all the glass-wares with care and avoid breaking them.
- Never mishandle & play with the equipments.
- Take & use only the glassware or tools needed for the experiment only.
- Every student will be allotted a working space no. at the beginning of the semester.
- Whenever in the lab student should work in the allotted space only.
- If any broken glassware, spillage of chemicals or untidiness is observed, strict action or marks will be deducted from the student responsible for that space.
- Before leaving the Lab, make sure to wash and dry the tools you used.
- Maintain silence in the lab and be a professional.

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Surface tension

Surface tension:

Surface tension is a phenomenon in which the surface of the liquid is in contact with the gas.

The surface tension of a liquid is the energy required to increase the surface area.

Examples of surface tension are drops of water, insects walking on water and paper clips floating on water.

Surface tension is defined as the force acting at right angles to a line of unit length present in the surface

or

The force per unit length (dyne/cm) that must be applied parallel to the surface so as to counterbalance the net inward pull of molecules.

Surface tension is denoted by ‘γ’.

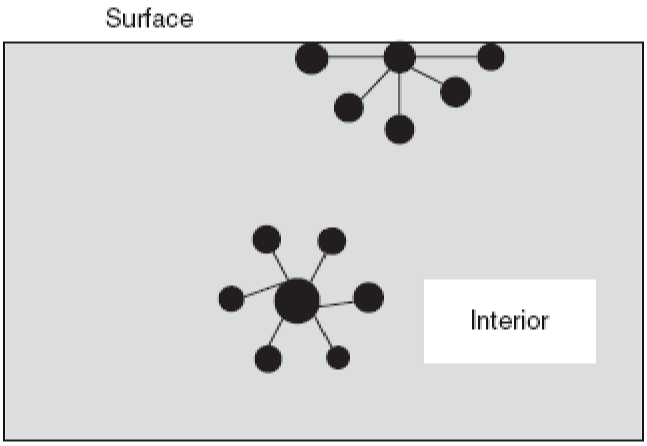
$$W = F \times d$$

Where
W = work; F = force; d = distance.

Therefore,

$$(\gamma)\ \text{Gamma} = F/d$$

The SI units for the surface tension are newton/meter or dyne/cm.
At a liquid surface, the molecule is not completely surrounded by other molecules.



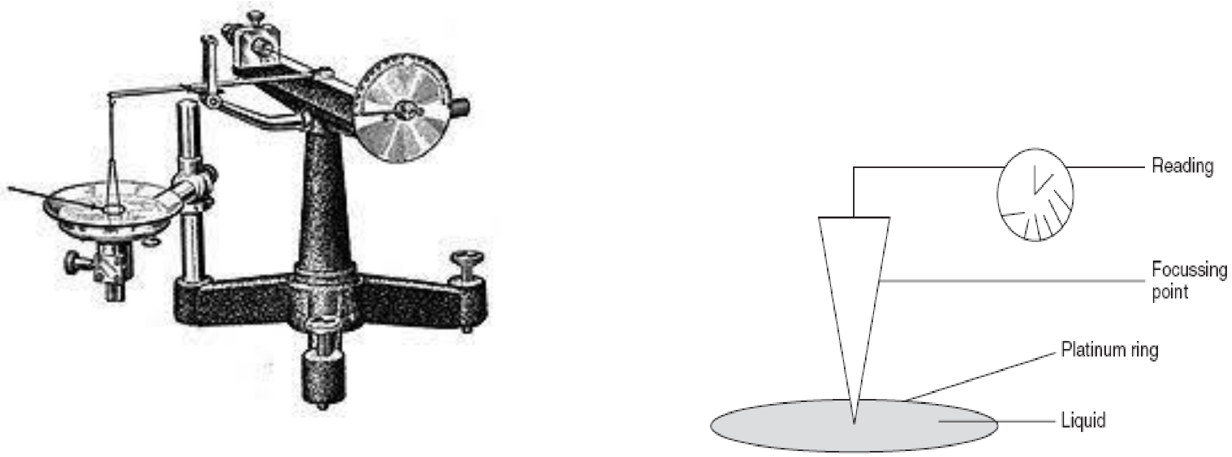
How to measure the surface tension

There are different methods for the determination of surface tension, as follows:

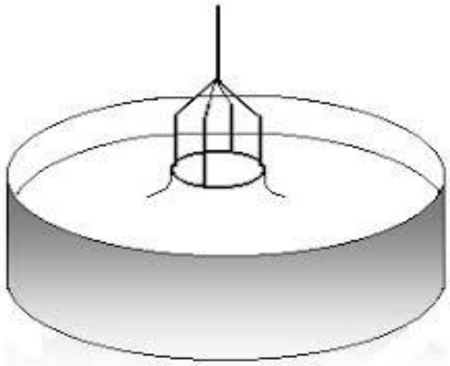
1- Du Nouy Ring Method

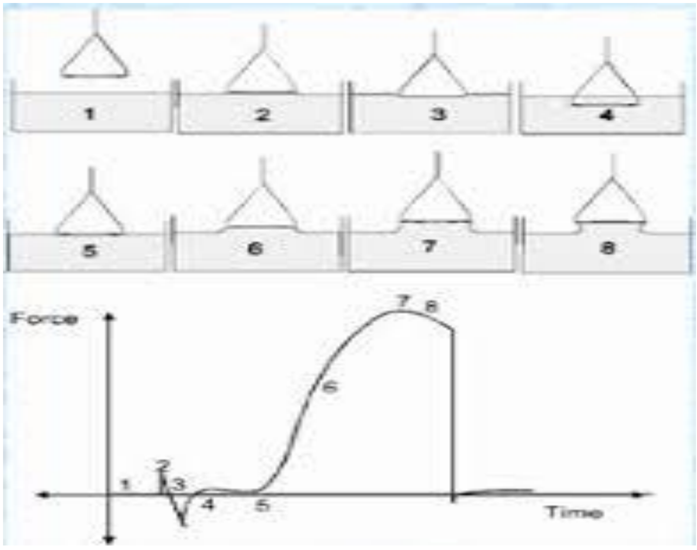
This method was first proposed by the Pierre Lecomte du Nouy in 1883. The basic principle involved in this method is lifting a ring from the surface of a liquid. Then the slow lifting of the ring which is made-up of platinum from the liquid surface is observed. The force required to raise the ring from the liquid surface is measured.

$$\gamma = (\text{dial readings in dynes}/2\ X\ \text{ring circumference})\ (\text{correction factor})$$



Du Nouy ring apparatus





2. Drop Shape Method

Surface tension is determined by fitting of the shape of the drop to the Young–Laplace equation:

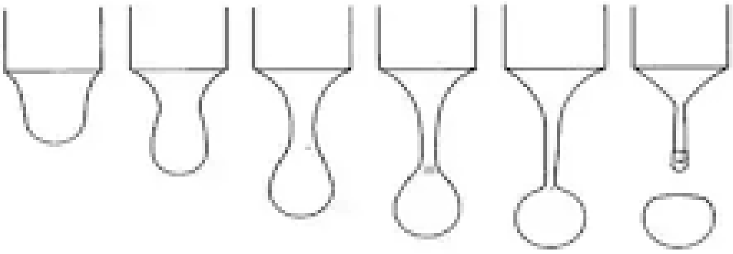
$$\Delta P = \gamma \, (1/R1 + 1/R2)$$

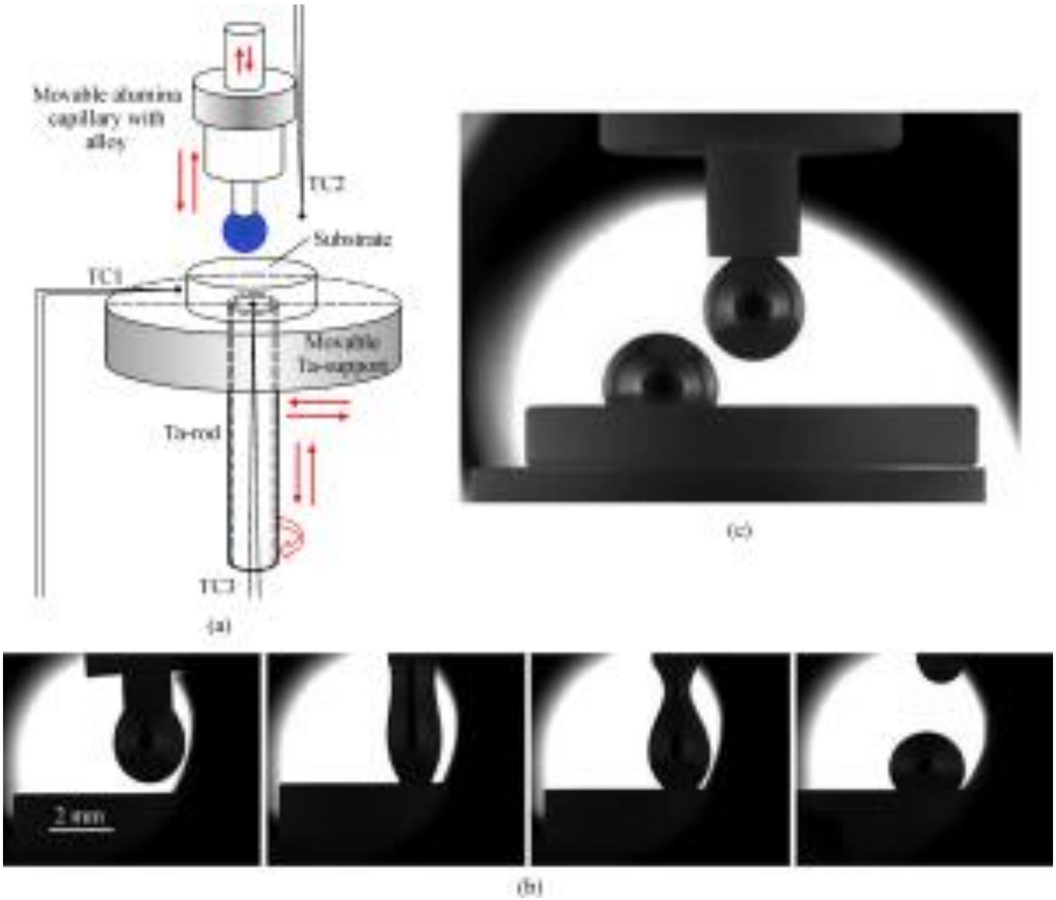
where

ΔP = pressure difference;

γ = surface tension;

R_1 and R_2 = surfaces radii of curvature.





(a)

(c)

(b)

3. Wilhelmy Plate Method

This method was first proposed by Ludwig Wilhelmy. A Wilhelmy plate is a thin plate used to measure equilibrium surface tension between the air–liquid or liquid–liquid interfaces.

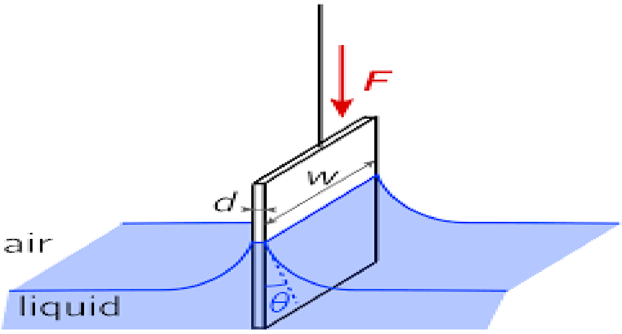
$$\gamma = F/l \cos\theta$$

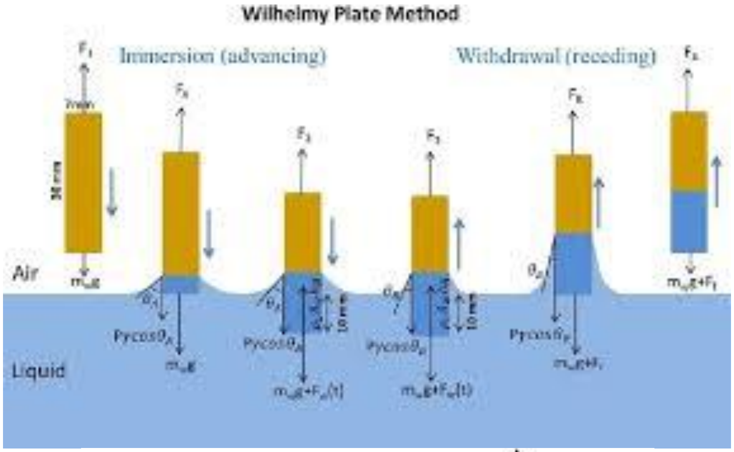
where

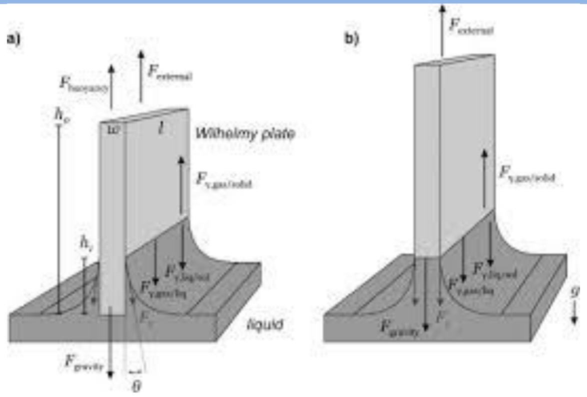
l = wetted perimeter of plate;

θ = contact angle between the interfaces of liquid and plate;

F = force.







4. Stalagmometric Method

The stalagmometer consists of the glass capillary tube specifically designed and calibrated for checking the surface tension of liquids.

Stalagmometers are graduated above and below their bulbs. They are available in 2.5mL, 3.5mL and 5.0mL sizes. The 2.5 and 5.0mL sizes allow flexibility in sample size of most liquid baths, while the 3.5mL size is used for more viscous applications.

The stalagmometer is filled with the sample solution and measures the weight of the drops or the number of drops. Based on this method, there are two methods for determination of surface tension:

1. Drop weight method
2. Drop number method

Drop weight method

Principle:

The drop of a mass **m** gets released when its weight G=mg is ≥ the surface force at the end of the tube.

$$m \cdot g = 2 \cdot \pi \cdot r \cdot \gamma \qquad (1)$$

Thus, by applying equation (1) γ can be calculated from the known water mass **m** and the radius of stalagmometer tube **r**.

However, it was shown experimentally that only about 2/3 of the drop volume gets released. In addition, this portion is not constant for all the drops. On the other hand, the ratio of the **m** and γ is constant for all the liquids. So

$$m_1 / \gamma_1 = m_2 / \gamma_2 \qquad (2)$$

Where m_1 and m_2 are the masses of drop 1 and 2 respectively, and γ_1 and γ_2 are the surface tensions corresponding to these liquids.

If the liquid with known γ is used for one of them (e.g. water γ_{H2O}), the γ of the other liquid can be calculated from equation.

$$\gamma = \gamma_{H2O} \,.\, m/m_{H2O} \qquad (3)$$

N.B:

You have to measure the mass of several drops in order to increase the precision of your measurements.

Table 1: The temperature dependence of the surface tension and distilled water density.

t °C	γ (N/m)	ρ_{H2O} (Kg/m^3)
15	**0.07349**	**999.96**
16	**0.07334**	**999.94**
17	**0.07319**	**999.90**
18	**0.07305**	**999.85**
19	**0.07290**	**999.78**
20	**0.07275**	**998.20**
21	**0.07259**	**997.99**
22	**0.07244**	**997.77**
23	**0.072428**	**997.54**
24	**0.07213**	**997.30**
25	**0.07197**	**997.05**

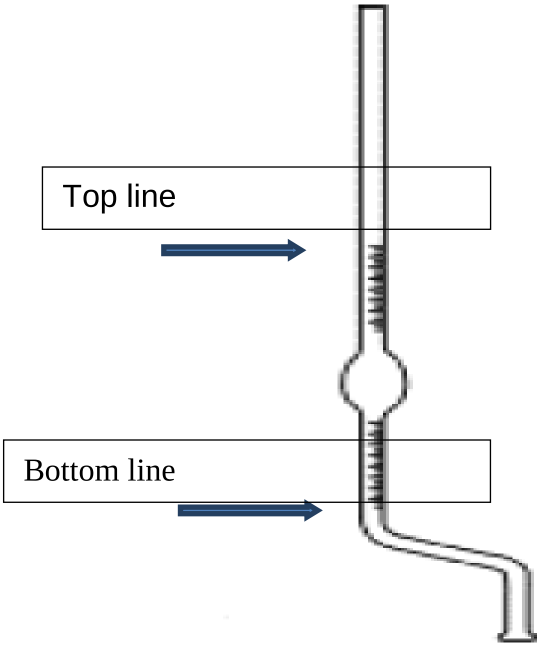
Determination of the surface tension by the drop-weight method.

Equipment's:

Stalagmometer, beaker, tubing with a balloon, weighing bottle with a lid, Analytical balance with the precision of the thousandth of gram, distilled (DI) water, liquids with the unknown surface tension.

Procedure:

1. Mount the clean and dry Stalagmometer on the vertical stand.
2. Weigh the mass of the weighing bottle m_0.
3. Fill the beaker with DI water. Mount the tubing with balloon on the top end of stalagmometer. Immerse the bottom end of stalagmometer into water and fill it up, such that the water level is above the wide part of stalagmometer.
4. Remove the balloon and collect **20** water drops into the weighing bottle.
5. Weigh the mass of the weighing bottle with water and determine the mass of 20 drops.
6. Empty the weighing bottle and stalagmometer, dry them and prepare for the next measurement.
7. Repeat steps 2-6 for liquids with the unknown surface tension.
8. Knowing the lab t^o, determine the γ_{H2O} using values from the table 1, and calculate the γ of unknown liquids according to the equation (3).



Stalagmometer with a calibrating scale

Results:

Liquid	weight of drops				γ (dyne/cm)
	W_1	W_2	W_3	W_{mean}	
Water					**72.8**
Liquid (A)					
Liquid (B)					

Drop number method

Principle:

The volume between the two lines in the Stalgmometer is **V**, and liquid with density ρ contained in this volume has a mass **m.**

$$\mathbf{m = V \cdot \rho} \qquad (1)$$

V depends on **n** drops.

The average mass of one drop is equation

$$\frac{m}{n} = \frac{V \cdot \rho}{n} \qquad (2)$$

Substituting the mass m in the equation (1) with the mass of one drop then yields equation

$$\gamma = \gamma_{H2O} \cdot \rho / \rho_{H2O} \cdot \mathbf{n}_{H2O} \ /\mathbf{n} \qquad (3)$$

Determination of the surface tension by the drop-counting method.

Known volume of the liquid (between 2 marks) is allowed to fall as drops from the tip of the stalagmometer under the effect of gravity and the number of drops is counted.

$$\frac{\gamma_1}{\gamma_2} = \frac{n_2\ \rho_1}{n_1\ \rho_2}$$

For simplicity ρ_1 and ρ_2 can be disregarded if the reference liquid have density value close to those of the liquid under examination, therefore;

Where:

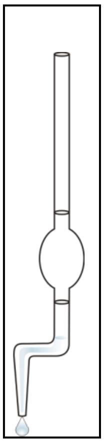
n_2 = Number of drops of the unknown liquid

n_1 = Number of drops of the water

γ_1 = Surface tension of the water

γ_2 = Surface tension of the unknown liquid

$$\frac{\gamma_1}{\gamma_2} = \frac{n_2}{n_1}$$



Procedures:

1. Wash the stalagmometer several times with water before use.
2. Apply a suction bulb to the upper tip of stalagmometer
3. Introduce the flat tip of the stalagmometer into a small beaker (100 ml) half filled with distilled water, suck water through the apparatus (avoiding entrance of air bubbles) till level of water is 1 cm above mark of the apparatus.
4. Using filter paper, remove any humidity on the outside of the apparatus.
5. Adjust level of water to the upper mark and remove any suspended drop.
6. Count the number of water drops falling until the level of water reaches the lower mark (the suspended drop is not counted).
7. Repeat the procedure 3 times for water and calculate the mean number of drops.
8. Repeat the above steps for liquid A and B after washing the apparatus twice with the liquid to be measured.

9. Record the results in the table below and use equation (2) to calculate the surface tension of liquid A and B.
10. Compare results obtained via the drop-weight method and drop counting method.

Results:

Liquid	**No. of drops**				**γ (dyne/cm)**
	n_1	**n_2**	**n_3**	**n_{mean}**	
Water					**72.8**
Liquid (A)					
Liquid (B)					

Determination of the Critical Micelle Concentration (CMC)

Principle

Surface active agents are molecules and ions that are adsorbed at interfaces, lowering the surface tension and decrease the contact angle between two phases.

Above a certain concentration range surfactant molecules cannot be accommodated with ease, they begin to agglomerate in the bulk of the solution forming aggregates called micelle.

The lowest concentration at which micelles first appear is called the critical micelle concentration (CMC).

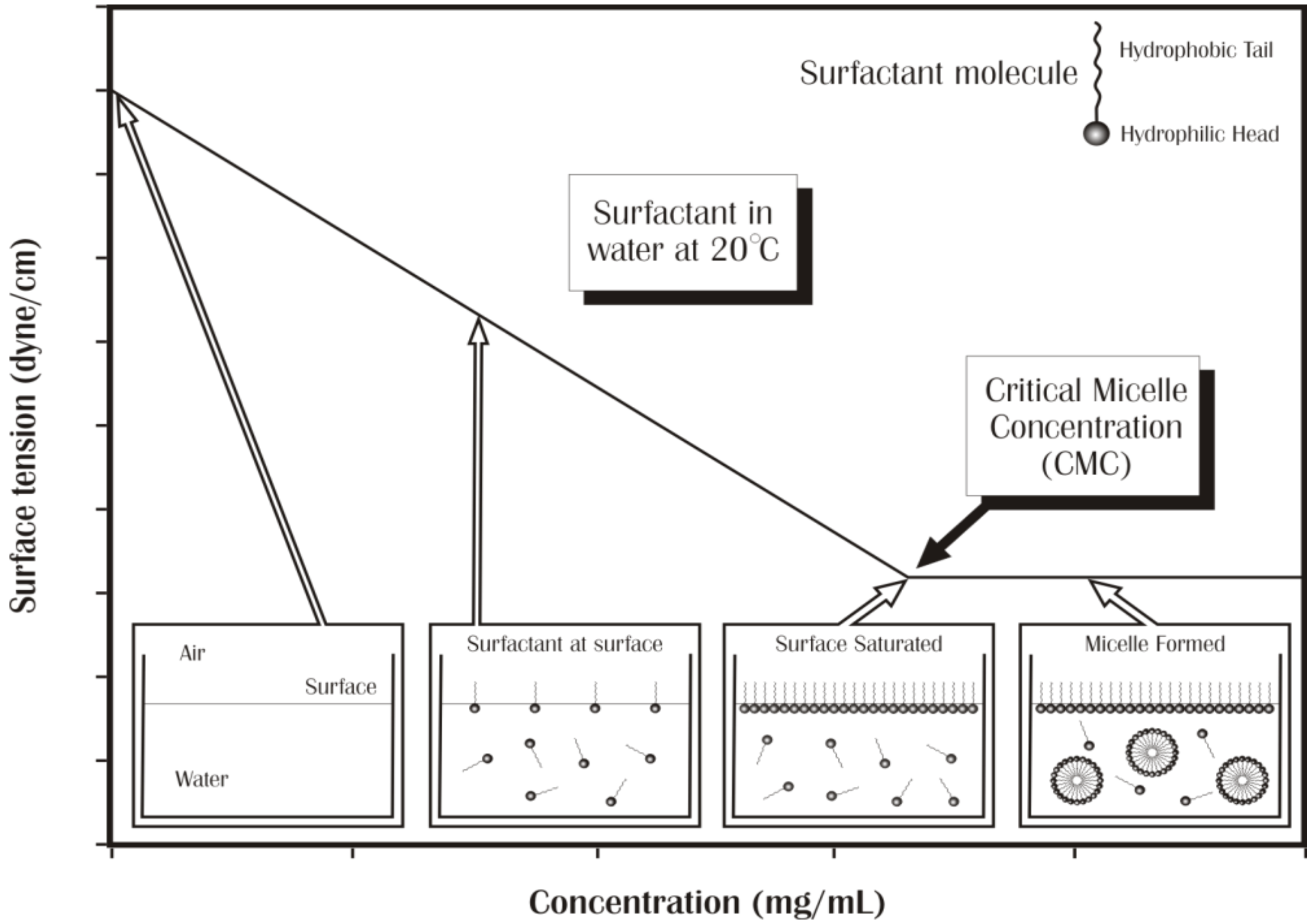


Figure 1: Surface tension curve as a function of surfactant concentration.

Initially the surfactant molecules increasingly arrange themselves at the water surface. During this phase the surface tension decreases linearly with the increase in surfactant concentration. When the CMC is reached, i.e. when the surface is saturated with surfactant molecules, a further increase in surfactant concentration no longer has any appreciable influence on the surface tension.

The CMC can be determined by the surface tension method:

When the surfactant concentration is plotted against its respective surface tension, the surface tension decrease with increasing surfactant concentration until the CMC is reached after which the surface tension is nearly constant.

The determination is based on the method of drop weight and drop volume method:

$$\frac{\gamma_1}{\gamma_2} = \frac{n_2}{n_1}$$

Procedure

You are provided with different concentrations of a surfactant A. Determine CMC as follows:

1. Wash the stalagmometer several times with water before use.
2. Apply a suction bulb to the upper tip of stalagmometer
3. Introduce the flat tip of the stalagmometer into a small beaker (100 ml capacity) half-filled with distilled water. Suck the water through the apparatus (avoiding entrance of air bubbles) till the level of water become above the upper mark of the apparatus by about 1cm.
4. Using a small filter paper remove any attached humidity of the outside the stalagmometer, adjust the level and remove any suspended drop.
5. Count the number of drops falling until the level of water reaches the lower mark (N_1).
6. Repeat the procedure for the different concentratios and determined the number of drops (N_2) after washing stalagmometer with water.
7. Tabulate your result and calculate the average surface tension for the given surfactant concentrations provided that the surface tension of water = 72.8 dyne/ cm.
8. Draw the curve between the surface tension on Y axis and the concentration of surfactant on X axis and determine CMC.

Results:

Liquid	Conc.	No. of drops				γ (dyne/cm)
		n_1	n_2	n_3	n_{mean}	
Water						**72.8**
Solution (1)						
Solution (2)						
Solution (3)						
Solution (4)						
Solution (5)						

Comment:

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Micellar Solubilization of Salicylic acid

Aim:

Examining the effect of surface active agent (SAA) on the solubility of sparingly soluble drugs (here: Salicylic acid).

Salicylic acid solubility is (2-2.5 gm /1L) of pure water

Introduction:

Water is a very powerful solvent. Water-SAA solution is used in the field of Pharmaceutics to make dosage forms containing sparingly soluble drugs. Generally, the degree of solubilization is a function of the physiochemical properties of the SAA and solubilized drug.

One of the properties of SAA is the ability to increase the solubility of a sparingly soluble drug through micelle formation. At concentrations above CMC an increase in solubility can be observed due to the micelle formation. As the number of micelles increases, the amount of soluble drug increased. Let us prove this

Solubilization of Salicylic Acid by Tween 80:

Tween 80, Mw = 1310 g/mol. CMC ~ 0.012mM = 13-15mg/L

Experimental:

Work in group. Each student will do the experiment at 2 different **tween 80** concentrations, then you share data with the group.

1. Number 6 clean 25 m1 beakers (1-6).
2. Place 250 mg of salicylic acid in each beaker.
3. To each beaker add 25 ml of Tween 80 (0%, 1%, 4% 8% and 10%).
4. Shake well for 10 min. this will produce 1% salicylic acid (if the total amount dissolved).
5. Filter the solution of each beaker.
6. Take 10 ml of each filtrate and titrate against 0.05 N sodium hydroxide solution using Phenol Phthalin indicator till the first pink color appear.

7. Determine the concentration of salicylic acid (SA) dissolved in each sample

Chemical factor;

0.0069 grams of salicylic acid is equivalent to 1 ml of 0.05 N sod.hydroxide.

i.e

1 ml of 0.05 N Sod. Hydroxide ≡ 0.0069 grams of salicylic acid

E.P ≡ ??? grams of salicylic acid

Chemical factor x E.P = grams of salicylic acid dissolved in 10 ml

II. Experimental Data and Results

Concentration of tween 80	E.P in ml	grams of salicylic acid in 10 ml= E.P x 0.0069	grams of salicylic acid in 1L =
0% tween 80	3.3	0.02277 gm	2.277 gm
1% tween 80			
4% tween 80			
8 % tween 80			
10 % tween 80	15.5	0.1069	10.69 gm

Measuring the viscosity of liquids and solutions

Viscosity is an important parameter that relates to texture and appearance of food and hence sensory experience while eating. Viscosity is also important in the rate of fluid flow and the amount of energy that may be required to move liquids in pipes. As it relates to fluid flow, there are generally two types. There is **Newtonian flow** and **Non-Newtonian** flow. When you think of Newtonian flow you can think of water and similar non-viscous fluids like beverages and wines. Regardless of how much shear stress you add to these liquids, their **viscosity** remains the same. Viscosity refers to the resistance of flow of a liquid. **Shear stress** is the force applied to the liquid, for example when we shake, mix or pump it. When we apply a shear stress we cause the liquid to move at a certain **shear rate** i.e. the velocity at which they flow. If you increase the speed of your blender for example, you are increasing shear force on the liquid which will cause it to move at a faster rate. In Newtonian fluids the thickness or viscosity will not change no matter how fast you mix the fluid.

Non-Newtonian fluids do not function the same way. They may change their viscosity depending on the amount of shear stress applied. Take for example ketchup. This fluid will behave like a solid until a force is applied to move it. That is why your ketchup will remain stuck in the bottle even when you turn it upside down. But as soon as you shake it, it starts to flow. Starch/water mixture is also Non-Newtonian. It becomes extremely viscous behaving like a solid when a very high shear force is applied but behave like a liquid when the force is removed.

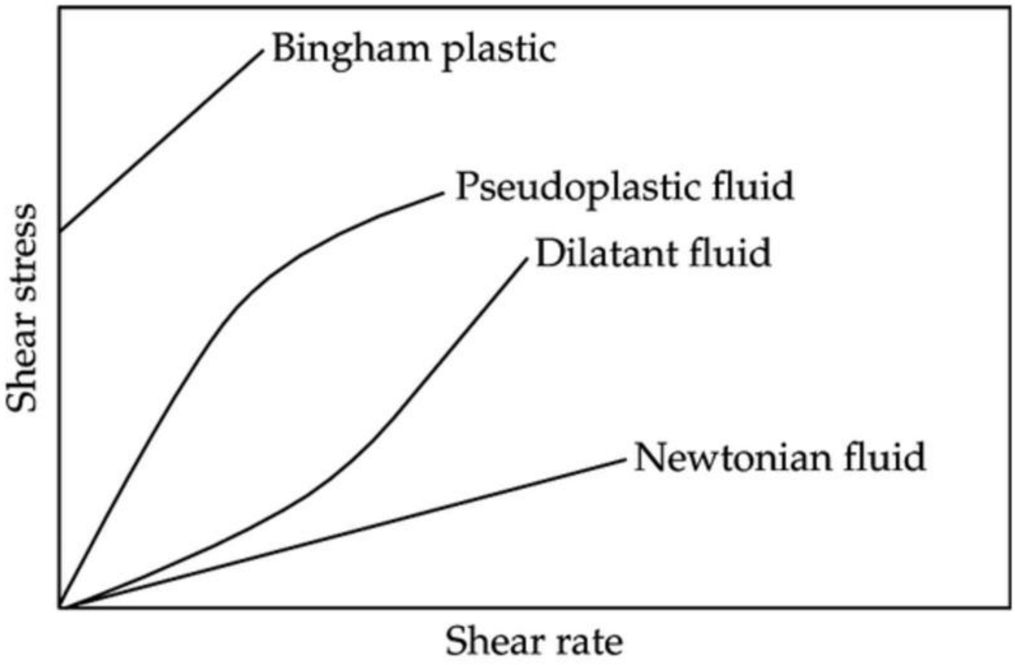
Types of Non-Newtonian Flow

Non-Newtonian flow can be broken down into various types as follows:

Pseudoplastic fluids – Fluids that display a *shear-thinning* behavior. That means the more stress you apply the faster they flow. Pseudoplastic fluids that are depended on time are called **thixotropic**. For these fluids if you maintain a constant stress, the fluid will still get *less viscous* over time. Example of fluids showing pseudoplastic behavior include concentrated fruit juices, egg white, mayonnaise, yogurt and sour cream

Dilatant fluids – Fluids that display a shear thickening behavior. That means the more you apply a stress, the more the fluid thickens. Dilatant fluids that are depended on time are called **rheopectic**. For these fluids, if you
Newtonion and Non-Newtonion Fluidsmaintain the same shear stress, it will still get thicker over time. Example of fluids showing dilatant behaviors include wheat flour dough and corn starch in water.

Bingham Plastic – Fluids that will not move until a minimum amount of force is applied. However, once they begin to flow they behave like a Newtonian fluid e.g. ketchup



Determination of the relative viscosity of Newtonian liquids and solutions

Principle

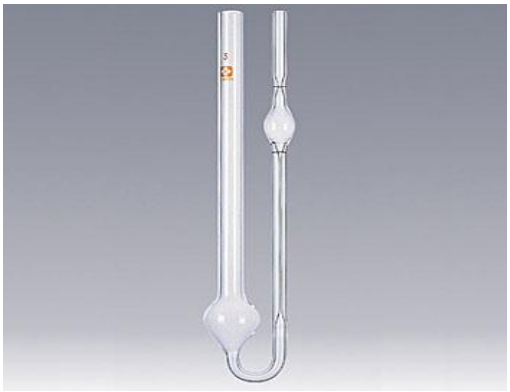
Capillary Viscometer

The viscosity of a Newtonian liquid may be determined by measuring the time required for the liquid to pass between two marks as it flows by gravity through a vertical capillary tube, known as an Ostwald viscometer

The time of flow of the liquid under test is compared with the time required for a liquid of known viscosity (usually water) to pass between the two marks

If η_1 nd η_2 are the viscosities of the unknown and the standard liquids, and t_1, and t_2 are the respective flow times in seconds, the viscosity $\eta_1$of the unknown liquid is called the relative η, is determined by substituting the experimental values in the equation

$$\frac{\eta_1}{\eta_2} = \frac{t_1}{t_2}$$



Materials and Method

Ostwald viscometer, suction bulb, syringe, distilled water, unknown samples

The sample is loaded into Ostwald viscometer. The time required for the sample to flow between two points on the viscometer is used to calculate the relative, viscosity.

1. Apply the suction bulb to tube B make suction to draw the sample through the capillary to a level of the start mark
2. Remove the suction bulb and measure the efflux time from starting mark to the stop mark (in seconds).

3. The above procedure is done for both distilled water and the unknown samples each for three times and the mean of the three results is calculated
4. Put your results in table and calculate the relative viscosity in centipoises for each sample.
5. Calculate the relative viscosity in centipoises using the following simple relation

$$\frac{\eta_1}{\eta_2} = \frac{t_1}{t_2}$$

where

η_1 = viscosity of unknown sample

η_2 = viscosity of water

t_1 = the time in seconds of flow of unknown sample

t_2 = the time in seconds of flow of water

Results:

Liquid	the time of flow				**η** (cps)
	t_1	**t_2**	**t_3**	**t_{mean}**	
Water					**1**(cps)
Liquid A (……………….)					
Liquid B (……………….)					

Determination of M.wt of a polymer by viscometery (viscosity average molecular weight)

Principle:

When a polymer dissolves in a solvent, the viscosity of the solvent increases and polymer chain has direct influence. Hermanan studinger reported a relationship between polymer M.wt and the relative magnitude of increase of viscosity

If the bulk volume of the viscometer is fixed, (t and t_0) are the flow rates and (η and η_0) are the viscosities of polymer solution and pure solvent. The ratio

$$t / t_0 = \eta / \eta_0$$

Since the lower limit of η_{rel} is unity, the specific viscosity η_{sp} which defines the relative increase in viscosity brought about by dissolved polymer molecules

$$\eta_{sp} = \eta_{rel} — \eta_0 / \eta_0 = (\eta_{rel} — 1)$$

The reduced viscosity (η_{red}) is obtained by relating (η_{sp}) to concentration C.

$$\eta_{red} = \eta_{sp}/C$$

Method

Using water as a solvent to prepare different concentrations of a hydrophilic polymer A as seen in the table below

Calculate $\eta_{rel.}$, η_{sp} .and $\eta_{red.}$ For each solution and put the results in table

Conc. Of polymer solution in water solvent (C)	$\eta_{rel.}$ $t/t_0 = \eta_{rel} / \eta_0$ $\eta_0 = 1$	$\eta_{sp.}$ $\eta_{sp} = (\eta_{rel} - 1)$	$\eta_{red.}$ $\eta_{red} = \eta_{sp}/C$
0.001 gm/dL			
0.002 gm/dL			
0.003 gm/dL			
0.004 gm/dL			
0.005 gm/dL			

Using a regular graph paper drew the (η_{red}) values for the different polymer concentrations on Y axis against conc (C). on X axis.

Extrapolate the produced line to intersect with the Y axis to get the value of (η_{red}) at zero concentration which is the intrinsic viscosity.

Apply in the Mark-Houwink equation to get the moleculer weight

From this equation the molecular weight of a polymer can be determined from data on the intrinsic viscosity and vice versa.

$$\eta_{int.} = K.M^{a}$$

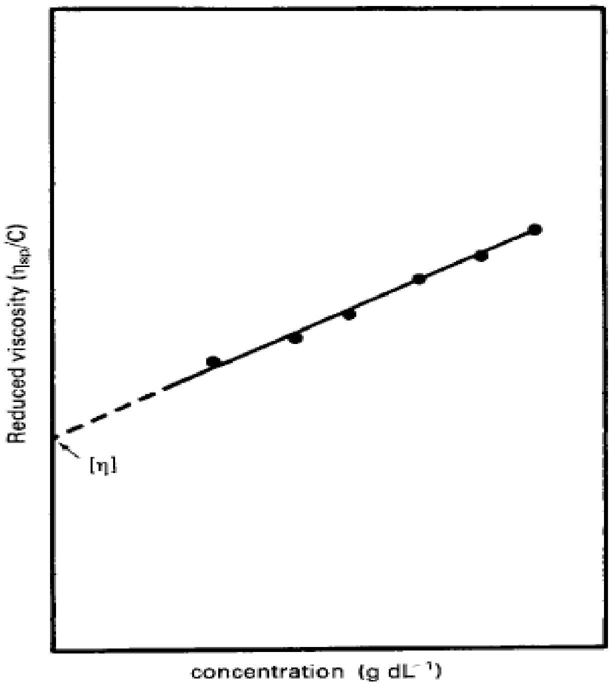
where :

η_{int} is the volume of polymer molecule in a given solvent

M is the viscosity average molecular weight

(**K** and **a**) are constants which describe the influence of solvent on the viscosity average molecular weight

Values of (**a**) factor of Mark-Houwink equation are typically between 0.5 and 0.8



Plot of concentration (g dL-1) against reduced viscosity η_{red} which by extrapolation gives the intrinsic viscosity η_{int}

For the polymer used

a= 1 and $K=10^3$

η_{int} = from figure

M=??

Results

………

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Kinetics of drug degradation

For patient safety we need to ensure that drug product provided to patients meet quality standards. The safety and effectiveness of any pharmaceutical product is associated with its stability through its usual Shelf-Life.

Herein, we studying the drug stability and assessing quantitatively the rate and order of drug degradation.

- **Rate of the Degradation**

  Can be expressed as the decrease in products concentration corresponding change in time

$$\pm \Delta C / \Delta t$$

- **Order of Degradation**:

  It is the manner in which the rate of degradation is influenced by the initial concentration of the products.

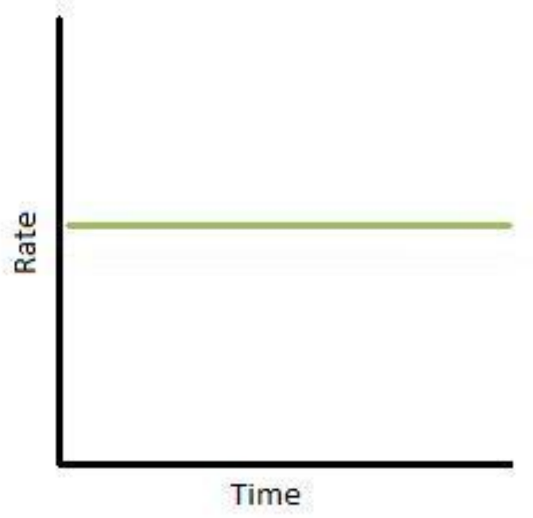
Order of degradation is classified into:

1- Zero-order
2- First-order
3- Second-order

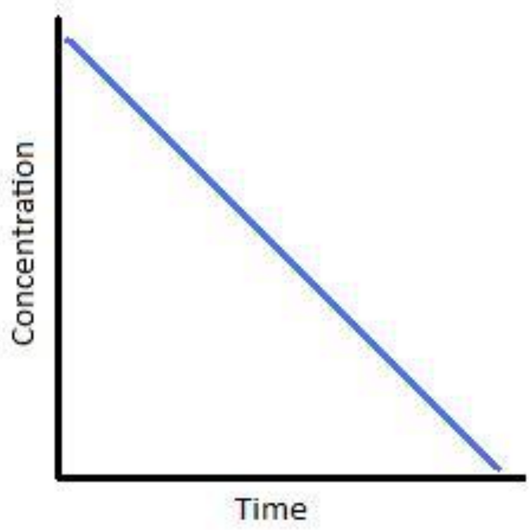
Zero-order Degradation

The rate is independent of the concentration. The rates of these **zero-order degradations** do not vary with increasing nor decreasing concentrations. This means that the rate of the degradation is constant.

$$- dc/dt = k$$



$$C_t = C_o - k_o t$$



$$t_{1/2} = C_o/2K$$

The half-life **depends** on the initial concentration. Increase the initial concentration increase the half-life and vice versa.

Problems:

1. **Determine the rate constant k of zero-order degradation if the initial concentration of Drug A is 1.5 mg and after 120 seconds the concentration of drug A is 0.75 mg.**

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   What is the half-life of Drug A if its original concentration is 1.2 mg?

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   If the original concentration is reduced to 1.0 mg, does the half-life decrease, increase, or stay the same? If the half-life changes what is the new half-life?

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Given is the rate constants *k* of three different reactions:

Drug A: $k = 2.3\ mg^{-1}s^{-1}$
Drug B: $k = 1.8\ mg/s$
Drug C: $k = 0.75\ s^{-1}$

Which reaction represents a zero-order reaction?

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First-order Degradation

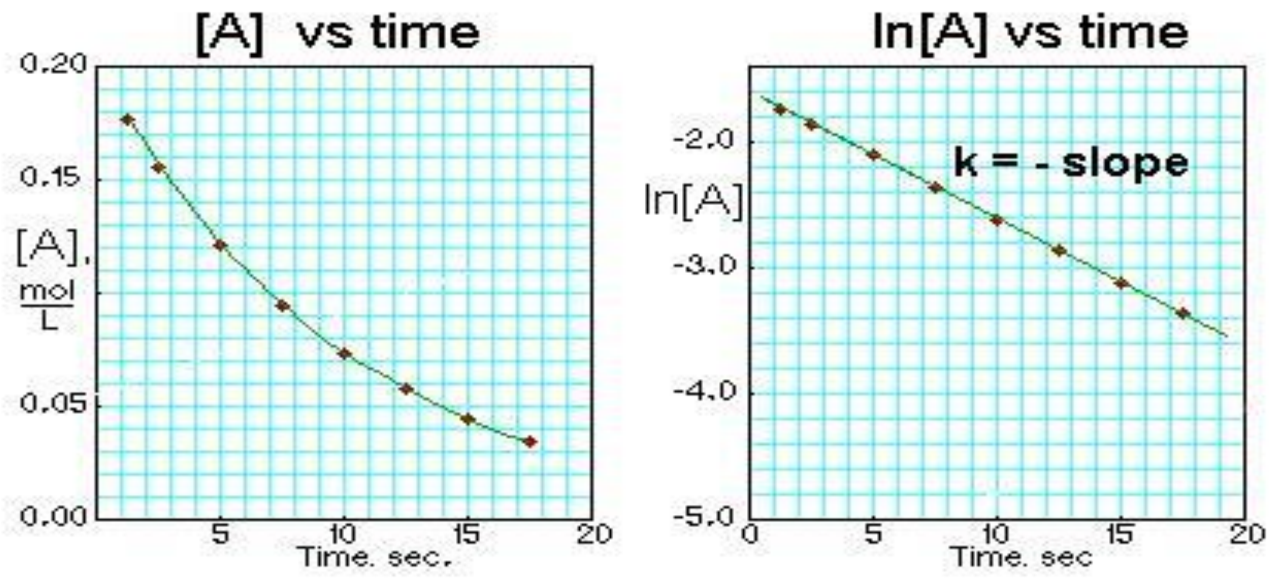
The rate is dependent of the concentration. The rates of these **first-order degradations** increase with increasing drug concentrations. This means that the rate of the degradation is not constant.

$$- dc/dt = kC$$

$$\text{Lin } C_t = \text{Lin } C_o\text{-}kt$$

$$\text{Log } C_t = \text{Log } C_o\text{-}kt/2.303$$

$$C_t = C_o\, e^{-kt}$$



$$t_{1/2} = 0.693/K$$

The half-life **does not depend** on the initial concentration and is constant.

Problems

1. **Determine the rate constant *k* and half-life of drug has a first-order degradation pattern if the initial concentration of Drug is 2.5 mg and after 10 months the concentration of the drug is 1.75 mg.**

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If the original concentration is reduced to 1.0 mg, does the half-life decrease, increase, or stay the same? If the half-life changes what is the new half-life?

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2. Calculate the half-life of the first order degradation below:

(a) If 4.00 g drug are allowed to decompose for 40 min, the mass of drug remaining undecomposed is found to be 0.80 g.

(b) If 8.00 g drug are allowed to decompose for 34 min, the mass of drug remaining undecomposed is found to be 0.70 g.

(c) If 9.00 g drug are allowed to decompose for 24 min, the mass of drug A remaining undecomposed is found to be 0.50 g.

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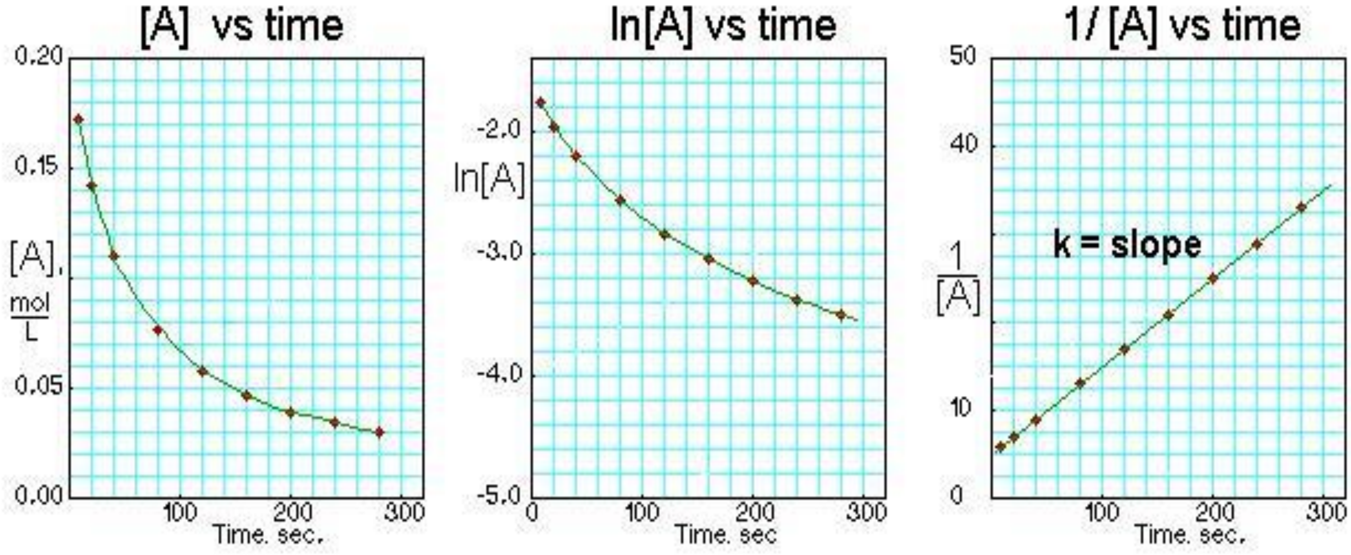
Second-order Degradation

The rate of degradation is dependent upon the initial concentration of two products

$$1/C_t = 1/C_o + 2kt$$



$$t_{1/2} = 1/\ C_oK$$

The half-life **depends** on the initial concentration. Increase the initial concentration decrease the half-life and vice versa.

Assignment

1. **Ofloxacin degrades by zero-order process with a rate constant of 0.05 mg/ml.year at room temperature. If 1%w/v solution is prepared and stored at room temperature, what concentration will remain after 18 months?**

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What is the half-life of Ofloxacin?

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2. 10 ml aqueous solutions of Amoxacillin (10%w/v) and Ampicillin (25%w/v) are stored in two identical test tubes under identical storage condition at 37°C for 3 months. If both drugs degrade by first-order, which drug will retain the highest percentage of initial concentration?

a. Amoxacillin
b. Ampicillin
c. They will be the same.

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3. The concentration of Vitamin D in aqueous solution drops by 10% per month when stored at room temperature. If the degradation occurs by first order, what concentration will remain if a 5 mg/ml solution of the drug is stored under the same condition for 3 months?

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4. A 5 g/100 ml solution of Amphotericin B is stored in a closed test tube at 25°C. If the rate of Amphotericin B degradation is 0.05 g/day, calculate the time required for initial concentration to drop to

(A) 90% of its initial concentration (shelf life).
(B) 50% of its initial concentration (half life).

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5. A 10 g/100 ml solution of Nystatin is stored in a closed test tube at 37°C. If the rate of Amphotericin B degradation is 0.1 mg/hr, calculate the time required for initial concentration to drop to 25 mg/ml.

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6. What is the remaining concentration in mg/ml of a drug (initial concentration = 7 mg/ml) after a time equivalent to 3 half-lives assuming that the decomposition follows first-order kinetics?

a. 2.33
b. 3.5
c. 1.75
d. 0.875
e. 1.167

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7. The time taken for 5% of a drug to decompose by first-order kinetics is:

a. 0.022/*k*1
b. 0.051/*k*1
c. 0.105/*k*1
d. *k*1/0.051
e. 0.105 *k*1

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Determination of degradation order

The order of degradation can be determined by various methods including:

1. Substitution Method:

The data collected in the experimental kinetic study can be substituted in the equations of the different orders. When the calculated k values remain constant within the limits of experimental variation, the → degradation is considered to be of that order.

2. Graphic Method:

The data collected in the experimental kinetic study plot in graphs and observing which plot is straight line.

Accordingly straight line plot of:

- **Concentration** against **time**, the degradation is zero order.
- **Lin** or **Log concentration** against **time**, the degradation is first order.
- **1/concentration** against **time**, the degradation is second order.

3. Half-Life Method:

This method is depending on the relationship between **initial concentration** and **Half-Life**.

- If $\mathbf{t_{1/2}}$ increase with increasing the **initial concentration** and vise versa, the reaction is zero order.
- If $\mathbf{t_{1/2}}$ is constant does not change with changing the **initial concentration**, the reaction is firstorder.
- If $\mathbf{t_{1/2}}$ decrease with increasing the **initial concentration and vise versa**, the reaction is zero order.

Problem:

1. **The following are the degradation data for Diclofenac potassium in a liquid dosage form obtained from stability study.**

   What is the order of this degradation?
   Calculate the degradation rate constant (*k*), half life and expire date of Diclofenac potassium.

Time (months)	Conc.(mg/ml)
0	20
3	18.2
6	16.4
9	14.6
12	12.8
18	9.2
24	5.8

2. The following are the degradation data for Itraconazole in a liquid dosage form obtained from stability study.

What is the order of this degradation?

Calculate the degradation rate constant (*k*), half life and expire date of Itraconazole.

Time (days)	Conc. (µg/ml)
0	20
30	16.4
60	12.8
90	9.2

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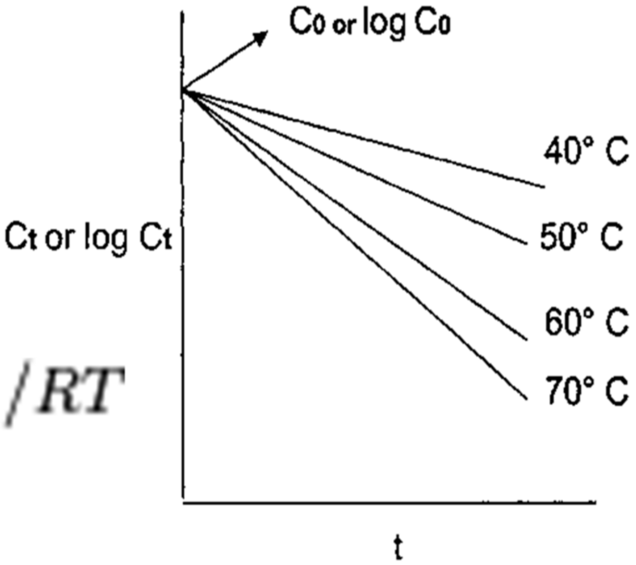
Accelerated stability study and Expiration dating

A method by which the drug is exposed to elevated temperature simulating what would happen over-longer periods on the shelf life to predict the shelf-life.

How to do?

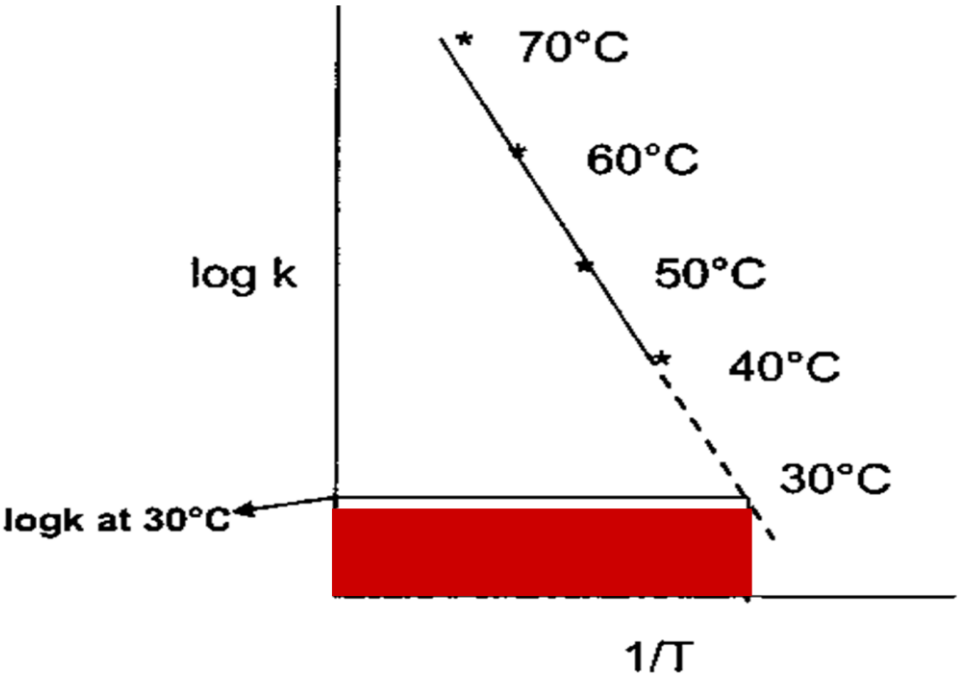
1. Store the liquid preparation of the drug at different elevated temperature, i.e 50 °C, 60°C, 70°C, 80°C, 100°C and 120°C.
2. At different time intervals, with draw samples from the stored drug (during the first year sample ever 3months, during the second year sample ever 6months and yearly after that).
3. Measure the drug content (concentration) in the withdrawn samples and plot the obtained concentration (as C or Log C) against the time, for the different temperature.

$$k = Ae^{-E_a/RT}$$



Accelerated breakdown of the drug at different elevated temperatures

4. Calculate the K values for the different temperatures and plot them as Log K against reciprocal of absolute temperature.
5. Extrapolate the obtained linear plot and determine the value of K_{25}.
6. Substitute the obtained K_{25}value in the equation of appropriate order to get the shelf life (**t_{90}**) of the drug under the normal shelf conditions.



Problem:

Given the data below for the decomposition of Clindamycin as a liquid dosage form

a. Calculate the activation energy for the reaction.

b. What is the value of the rate constant at 25 °C and the Expire date of this product?

T (K)	k (s^{-1})
343	7.2×10^{-4}
353	2.2×10^{-3}
363	1.7×10^{-2}
373	0.11

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Evaluation Sheet

Student Name: --

Student Number: ---

Working Space Number: ☐

Sl. No	Laboratory No	Date	Evaluation	Comment	Signature
1	Determination of the surface tension				
2	Determination of the Critical Micelle Concentration (CMC)				
3	Micellar Solubilization of Salicylic acid				
4	Determine the relative viscosity of Newtonian liquids and solutions				
5	Determination of viscosity average M.wt of a polymer.				
6	Kinetics of drug degradation				
7	▪ Determination of degradation order ▪ Accelerated stability study and Expiration dating				

Average Evaluation

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